Randi Bertelsen

Editor's Summary:

Several studies have reported links between asthma in children and the presence of phthalates in dust from the children's homes. But the presence of a chemical is not the same thing as exposure, so Norway's Environment and Childhood Asthma Study has taken the research a step farther by measuring phthalates in the urine of children with and without asthma. In this podcast Randi Bertelsen discusses her recently published findings.

Phthalates and Childhood Asthma, with Randi Bertelsen

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AHEARN: It's *The Researcher's Perspective*. I'm Ashley Ahearn.

Phthalates are used as plasticizers in a large number of consumer goods—from plastic toys to cosmetics and fragrances. These chemicals are also widespread in Americans, and they are associated with reproductive health problems in lab animals. But there may be more health effects at play. In a recent study published in *EHP*, researchers found an association between phthalate exposure in children and asthma and allergic disease.[1]

Joining me to talk about it is coauthor Randi Bertelsen. She is a visiting fellow in the Epidemiology Branch of the National Institute of Environmental Health Sciences. Randi, thanks for being here.

BERTELSEN: Thanks for inviting me.

AHEARN: Now, before we get into the specifics of your study, let's talk a little bit about phthalates themselves. There are many different kinds, but for the purpose of your research you focused on differences in the molecular weight. Why is that difference important, and what do we know about the exposures to various types of phthalates?

BERTELSEN: Well, yeah, the length of the alkyl chains leads to different molecular weights, and this also affects the functionality of the phthalates. So the functionality differs depending on whether they are high- or low-molecular-weight phthalates, and the high-molecular-weight phthalates are used as plasticizers in, like, PVC-containing products—typically flooring and other indoor building materials—in toys, in food packaging, in car interiors, and many other consumer products; and the low-molecular-weight phthalates are used in fragrances and other personal care products as well as in medications. And it is the high-molecular-weight phthalates that most often have been associated with respiratory disease.

But one of the biggest problems with phthalates is that they are not strongly bound to the materials to which they are added, so they are continuously released to their surroundings. So the low molecular weights are more likely to become airborne, and therefore inhalation may be an important route of exposure, but the high-molecular-weight phthalates may be more likely to be found in sediment and dust, and therefore, like, infants unintentionally digest the dust—actually, one of the most important sources of exposure to phthalates. And the use of plastics in food processing makes food a very important source of exposure to some of the higher-molecular-weight phthalates for adults.

AHEARN: Randi, tell me about your study. How was it conducted?

BERTELSEN: This study is part of the Environment and Childhood Asthma Study, which is an ongoing birth cohort study that recruited healthy infants at birth in Oslo in 1992 and 1993. So these are mainly ethnic Norwegian children, and approximately equal numbers of boys and girls have been followed up. And at 10 years of age these children were invited to participate in the followup study with very thorough clinical examination that also included collection of first-morning urine, and current asthma was diagnosed based on parental interview and exercise challenge testing. And for this particular study we included 623 children, and on purpose we oversampled the cases with asthma, so a total of 21% of the children in this study had current asthma at followup.[2]

And then we analyzed the urine samples for 11 phthalate metabolites in both high- and low-molecular-weight phthalates, and we used logistic regression modeling to estimate associations between the urinary concentrations of the phthalates and current asthma.

AHEARN: And what did you find?

BERTELSEN: Well, first of all we found that all of the 623 urine samples had detectable levels of all the 11 phthalate metabolites that we measured, and the levels were comparable to the levels that have been reported for children in the U.S. of comparable age. And we found that already at 10 years the girls had higher levels of urinary concentrations of the low-molecular-weight phthalates, which was a bit surprising.

AHEARN: Those are the phthalates that come from things like fragrances and perfumes, right, Randi?

BERTELSEN: That is correct. And we found that current asthma was associated with increased concentrations of metabolites from two high-molecular-weight phthalates, and these were the diisodecyl phthalate, or DIDP, and the diisononyl phthalate, DINP.

AHEARN: Phthalates are metabolized quickly. How does a snapshot of urine sample quantify or represent that ongoing exposure that these children have?

BERTELSEN: That is a good question. First of all, the advantage of measuring biomarkers is that they help us to identify the overall exposure regardless of the source, and this is a major advantage over, like, environmental or self-reported methods, and it gives us sort of a total picture of the body burden of exposure from all routes of exposure—like, from inhalation, from the oral exposure, and from what you get through the skin. But because they are so quickly metabolized in the body, the levels that we measure in one single urine sample are not necessarily representative of longtime exposure.

But this will also depend on the source, such as, for instance, exposures or metabolites of phthalates that come from cosmetic products are assumed to be more reliable since we tend to use the same cosmetic products for an extended period of time, but for metabolites from some of the phthalates that we believe are mainly exposure from contaminated food may show more variation from, for instance, day-to-day. So ideally, you would want to have more than one urine sample for each participant. But unfortunately this is not always the case, and the biological specimens are valuable, and you often only have one sample for one particular point in time.

AHEARN: Looking at your research, how strong is the association between phthalate exposure and asthma in these children?

BERTELSEN: Well, the association that we found was, it's only like a modest association, but what's been consistent between this study is that it's mainly the high-molecular-weight phthalates that have been associated with asthma or respiratory symptoms. But again, because these are cross-sectional studies, which means that we measure exposure at the same time as disease, we can never be sure of whether the associations that we are seeing are due to some particular behavior or characteristics among the asthmatic children compared to the nonasthmatic, such as, for instance, maybe the asthmatic children tend to have more plastic surfaces at home because they are easier to keep clean.

And at least in our study we did have very detailed information on treatment and use of medications. We tried to see whether the association that we were seeing was due to some— maybe the asthma medication. We didn't find any association between the levels of the phthalate metabolites in urine and the use of asthma medication that was taken the last few weeks and even the last few days before this clinical examination and urine collection. But then, of course, the epidemiological studies cannot tell us about the mechanisms, so more studies are needed before we can say that there is actually a causal association.

AHEARN: That was my next question for you, Randi: What do we know about the mechanisms here? What might be happening?

BERTELSEN: Actually, we know very little about how phthalates may affect respiratory disease, since most toxicological studies have focused on reproductive end points—because these are, of course, very important—and also because there are few animal models of asthma. And there are some animal models of allergy that found phthalates to enhance the production of IgE [immunoglobulin E], which is what leads to allergy, but the exposure levels where these effects were seen are so much higher than what has been observed for human exposure, and there are also few *in vitro* studies where they have reported phthalates to increase the production of some proinflammatory cytokines that are linked to asthma exacerbation, but there is so far no conclusive evidence.

AHEARN: Randi, thanks so much for joining me.

BERTELSEN: Thank you.

AHEARN: Randi Bertelsen is a visiting fellow in the Epidemiology Branch of the National Institute of Environmental Health Sciences.

And that's *The Researcher's Perspective*. I'm Ashley Ahearn. Thanks for downloading.

Ashley Ahearn, host of *The Researcher's Perspective*, has been a producer and reporter for National Public Radio and an Annenberg Fellow at the University of Southern California specializing in science journalism.

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REFERENCE AND NOTE

1. Bertelsen RJ, et al. Urinary biomarkers for phthalates associated with asthma in Norwegian children. Environ Health Perspect 121(2):251–256 (2013); http://dx.doi.org/10.1289/ehp.1205256.
2. Asthma has been estimated to affect 5–11% of Norwegian 10-year-olds, according to the Norwegian Institute of Public Health.